

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Obesity and NAFLD: Mechanisms and Therapeutics (B3)

February 23-27, 2020 • Fairmont Banff Springs • Banff, AB, Canada

Scientific Organizers: Rebecca A. Haeusler, Shingo Kajimura and Alexei Kharitonov

Sponsored by AstraZeneca, Gilead Sciences, Inc., Merck & Co., Inc. and Novo Nordisk A/S

Discounted Abstract & Scholarship Deadline: October 23, 2019 / Abstract Deadline: November 21, 2019 / Discounted Registration Deadline: December 19, 2019

### SUNDAY, FEBRUARY 23

#### Arrival and Registration

### MONDAY, FEBRUARY 24

#### Welcome and Keynote Address

\***Rebecca A. Haeusler**, Columbia University, USA

**Mitchell A. Lazar**, Perelman School of Medicine, University of Pennsylvania, USA

*The Fourth Dimension of Obesity and NAFLD*

#### New Pathways in Hepatic Metabolism

\***Maaïke Oosterveer**, University Medical Center Groningen, Netherlands

**Kun-Liang Guan**, University of California, San Diego, USA

*The Hippo Pathway in Metabolism and Organ Growth*

**Hannele Yki-Järvinen**, University of Helsinki, Finland

*Function of the PNPLA3 I148M Gene Variant in the Human Liver*

**Mark A. Herman**, Duke University Medical Center, USA

*Molecular Aspects of Fructose-Induced Metabolic Dysregulation*

**Lei Yin**, University of Michigan Medical School, USA

*Short Talk: DDB1 E3 Ligase Links Dietary Fructose Intake and ChREBP Protein Stabilization and Enhanced De Novo Lipogenesis via CRY1 Degradation*

**Jennifer L. Estall**, Institut de Recherches Cliniques de Montréal, Canada

*Short Talk: Glucagon Enhances Insulin-Mediated Suppression of Gluconeogenesis by Regulating the IRS1:IRS2 Ratio via PGC1A*

#### Mitochondrial Function in Energy Balance and Metabolic Disease

\***Shingo Kajimura**, University of California, San Francisco, USA

**Brian N. Finck**, Washington University School of Medicine, USA

*Targeting Mitochondrial Intermediary Metabolism to Treat NAFLD*

**Maren C. Podszun**, NIDDK, National Institutes of Health, USA

*Short Talk: Vitamin E Treatment in NAFLD Reveals Novel Pathway: Oxidative Stress Drives De-Novo Lipogenesis Through S1P/S2P Proteases*

**Douglas G. Mashek**, University of Minnesota, USA

*Lipid Droplet Signaling as a Driver of Mitochondrial Metabolism*

**Jun Wu**, University of Michigan, USA

*Nicotinic Acetylcholine Receptors in Energy Metabolism*

**Lawrence Kazak**, McGill University, Canada

*Short Talk: Creatine Energetics in Brown Fat Controls Energy Expenditure through Creatine Kinase B-Type*

#### Poster Session 1

### TUESDAY, FEBRUARY 25

#### Metabolites Mediating Tissue Crosstalk

**Christopher B. Newgard**, Duke University Medical Center, USA  
*Hepatic Metabolic Regulatory Nodes Linked to Cardiometabolic Diseases*

**Claudio J. Villanueva**, University of California, Los Angeles, USA  
*Adipose-Liver Crosstalk and Adaptive Thermogenesis*

**Rebecca A. Haeusler**, Columbia University, USA  
*Bile Acid Regulation of Metabolism*

**Annelise Poss**, University of Utah, USA

*Short Talk: Ceramides as Lipotoxic Mediators of Non-Alcoholic Fatty Liver Disease and Steatohepatitis*

\***James C. Lo**, Weill Cornell Medicine, USA

*Short Talk: An Adipose Regulator of Beta Cell Failure*

**Maaïke Oosterveer**, University Medical Center Groningen, Netherlands

*Short Talk: Hepatic ChREBP Activation Limits NAFLD Development in a Mouse Model for GSD Ia*

**Kirk M. Habegger**, University of Alabama, Birmingham, USA

*Short Talk: Title to be Announced*

#### Workshop 1: Late-Breaking Research in Obesity and NAFLD

\***Claudio J. Villanueva**, University of California, Los Angeles, USA

**Andrea Galmozzi**, The Scripps Research Institute, USA

*Intracellular Heme Trafficking in Adipocytes Regulates Energy Homeostasis*

**Lucia Korinkova**, Czech Academy of Sciences, Czech Republic

*Impact of Lipidized Prolactin-Releasing Peptide Treatment on Metabolic Syndrome and Leptin-Related Signaling Pathways in Three Mouse Models*

**Ichiro Shimomura**, Osaka University, Japan

*Action Mechanism of High-Molecular Weight Multimer Adiponectin – Possible Role of Stem Cells, T-Cadherin, and Exosomes for Organ Protections*

**Mohammad Abu Odeh**, University of California, San Diego, USA

*FGF21 Acts Locally on the Adipose Tissue to Induce Weight Loss*

**Ludger Scheja**, University Medical Center Hamburg-Eppendorf, Germany

*The Role of the Alternative Pathway-Derived Bile Acids in NAFLD Progression*

**Abraham Stijn Meijnikman**, Amsterdam University Medical Center, Netherlands

*Hyperinsulinemia, a Key Player in Visceral Adipose Tissue and Hepatic Cellular Senescence*

**Yohei Kanamori**, Nagoya University, Japan

*Role of Iron in the Emergence of Proinflammatory and Profibrotic Macrophages in a Mouse Model of Nonalcoholic Steatohepatitis*

**WonGun Choi**, Korea Advanced Institute of Science and Technology, South Korea

*The Role of Serotonin Signaling through HTR2A/2B in Visceral Adipose Tissue*

#### Drivers of NAFLD and Dyslipidemia in Obesity

\***Masahiro Koseki**, Osaka University, Japan

**Elizabeth J. Parks**, University of Missouri, USA

*Liver Metabolic Flux in NAFLD and NASH*

**Greg Steinberg**, McMaster University, Canada

*Cellular Energy Sensing and Metabolism: Implications for Treating NAFLD*

**Lale Ozcan**, Columbia University, USA

*Glucagon-Mediated Regulation of Cholesterol Metabolism*

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**Onno Holleboom**, Amsterdam UMC, Netherlands

*Short Talk: Deficiency of V-ATPase Assembly Factors TMEM199 and CCDC115 Results in Hepatic Steatosis and Hyperlipidemia and May Affect Fusion of Lipid Droplets and Lysosomes*

**Maria Chondronikola**, University of California, Davis, USA

*Short Talk: Brown Adipose Tissue is Linked to Very-Low-Density Lipoprotein Triglyceride Metabolism in People*

### Poster Session 2

#### WEDNESDAY, FEBRUARY 26

##### Obesity Pathogenesis and New Protein Therapeutic Strategies

\***Raymond E. Soccio**, University of Pennsylvania, USA

**Alexei Kharitonkov**, Novo Nordisk, USA  
*Novel FGF21 Variants*

**Hank Mansbach**, 89bio, USA

*BIO89-100, a Long-Acting FG21 Analog, for Treatment of NASH and Cardio-Metabolic Disorders*

**Timothy Rolph**, Akero Therapeutics, Inc., USA

*Short Talk: AKR-001, a Long-Acting, Degradation-Resistant FGF21 Analog, Elicits Sustained Improvements in Markers of Glycemic Control and Lipid Metabolism in a 4-Week, Multiple Ascending Dose Study*

**Maria E. Wilson**, Genentech, Inc., USA

*Short Talk: An Anti-FGFR1/KLB Bispecific Antibody Improves Lipid Profile, Markers of Fibrogenesis, and Liver Health in Patients with Type 2 Diabetes (T2DM) and Decreases Hepatic Fat in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD)*

**Lotte Bjerre Knudsen**, Novo Nordisk A/S, Denmark

*GLP-1 Receptor Agonists: Mechanisms Relevant for the Treatment of Obesity and NASH*

**Asger Bach Lund**, University of Copenhagen, Denmark

*Short Talk: The Effects of GIP on Food Intake, Energy Expenditure and Plasma Glucose in Patients with Type 2 Diabetes Treated with a Long-acting GLP-1 Receptor Agonist*

**Bruce L. Riser**, BLR Bio, USA

*Short Talk: CCN3-Based Peptide Inhibits/Reverses Liver Injury in a Mouse Model of Diabetes and Obesity*

**Magdalene K. Montgomery**, University of Melbourne, Australia

*Short Talk: Arylsulfatase A (ARSA) is a Novel NASH-Regulated Hepatokine and Potent Regulator of Glycaemic Control*

##### Pathogenesis of NASH and Liver Fibrosis

\***Yaron Rotman**, NIDDK, National Institutes of Health, USA

**Bart Staels**, Institut Pasteur de Lille, Université Lille, France

*Pathways in the Transition of Fatty Liver to Active Disease NASH*

**Utpal B. Pajvani**, Columbia University Medical Center, USA

*Hepatocyte Jagged-Notch Signaling Induces Fibrosis in NASH*

**Anna Mae Diehl**, Duke University, USA

*Fixing Fatty Livers*

**Charlotte L. Scott**, University of Ghent & VIB, Belgium

*Short Talk: Lipid-Associated Stress Results in a Loss of Kupffer Cells from the Liver in NAFLD and Repopulation of the Niche by Fatty Liver Associated Macrophages*

### Poster Session 3

#### THURSDAY, FEBRUARY 27

##### Adipose Tissue and Organismal Energy Balance

\***Christian Wolfrum**, ETH Zürich, Switzerland

**Shingo Kajimura**, University of California, San Francisco, USA  
*The Roles of Brown Adipose Tissue Beyond Thermogenesis*

**Karine Clément**, INSERM / Sorbonne Université, France  
*Origins of Adipose Tissue Fibrosis*

**Alexander S. Banks**, Harvard Medical School, USA

*Obesity-Linked PPAR $\gamma$  S273 Phosphorylation Promotes Insulin Resistance through Growth Differentiation Factor 3*

**Silvia Corvera**, University of Massachusetts Medical School, USA  
*Mechanisms Controlling Number and Type of Adipocytes*

**Joerg Heeren**, University Medical Center Hamburg-Eppendorf, Germany

*Short Talk: Endothelial Lysosomal Acid Lipase Deficiency Impairs White Adipose Tissue Browning*

**Alexander Paul Sakers**, University of Pennsylvania, USA

*Short Talk: Lineage Specification of Perivascular Thermogenic Adipocytes*

##### Workshop 2: Late-Breaking Drug Targets

\***Shirly Pinto**, Kallyope, USA

**Victor Leonard Schuster**, Albert Einstein College of Medicine, USA  
*Inhibiting the Prostaglandin Transporter PGT Induces Non-Canonical Thermogenesis at Thermoneutrality*

**Cecile Vernochet**, Pfizer, USA

*Adipose GI Signaling is Essential for Liver Fat and Whole Body Glucose Homeostasis*

**Shengping Wang**, Johnson and Johnson, USA

*Weight Loss Via Caloric Restriction Resolves Non-Alcoholic Steatohepatitis (NASH) in Cynomolgus Monkeys*

**Eva C. Thoma**, Insphero AG, Switzerland

*Establishment of a 3D Human NASH Model for High-Throughput Drug Efficacy Testing*

**Caslin Anne Gilroy**, University of California at Berkeley, USA

*The Metabolic microRNA miR-128-1 as a Therapeutic Target for the Treatment of NASH*

**Jean-Francois Thibodeau**, Liminal R&D BioSciences Inc., Canada  
*PBI-4050: A Free Fatty Acid Mimetic for the Treatment of NAFLD*

**Jerome Deval**, Aligos Therapeutics, USA

*Preclinical Development of ALG-055009 as a Potent and Selective Thyroid Hormone Receptor Beta Agonist for the Treatment of NASH*

**Jin Zhou**, Duke-NUS Medical School, Singapore

*Thyroid Hormone Decreases Hepatic Steatosis, Inflammation, and Fibrosis in a Dietary Mouse Model of Non-Alcoholic Steatohepatitis (NASH)*

##### Obesity & NAFLD: Bridging Basic Discoveries and Clinical Application

\***Rebecca A. Haeusler**, Columbia University, USA

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**Robert K. Semple**, University of Edinburgh, UK  
*Mechanisms Linking Human Adipose Tissue, Insulin Resistance and Fatty Liver: Insights from Human Genetics*

**Jan Borén**, University of Gothenburg, Sweden  
*Novel Interventions for NAFLD*

**Brian Finan**, Novo Nordisk, USA  
*Peptide Tri Agonists for the Treatment of Obesity and Diabetes*

**Emelie Barreby**, Karolinska Institutet, Sweden  
*Short Talk: Characterization of Distinct Populations of Liver Macrophages in Obesity and Insulin Resistance*

**Meeting Wrap-Up: Outcomes and Future Directions (Organizers)**

**FRIDAY, FEBRUARY 28**

**Departure**